ClinicalEvidence

Kidney stones: flexible ureteroscopy

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ABSTRACT

INTRODUCTION: The age of peak incidence for stone disease is 20 to 40 years, although stones are seen in all age groups. There is a male to female ratio of 3:2. METHODS AND OUTCOMES: We conducted a systematic overview, aiming to answer the following clinical question: What are the effects of flexible ureteroscopy for the removal of renal stones? We searched: Medline, Embase, The Cochrane Library, and other important databases up to May 2014 (BMJ Clinical Evidence overviews are updated periodically; please check our website for the most up-to-date version of this overview). RESULTS: At this update, searching of electronic databases retrieved 197 studies. After deduplication and removal of conference abstracts, 118 records were screened for inclusion in the overview. Appraisal of titles and abstracts led to the exclusion of 99 studies and the further review of 18 full publications. Of the 18 full articles evaluated, one systematic review and four RCTs were added at this update. We performed a GRADE evaluation for eight PICO combinations. CONCLUSIONS: In this systematic overview, we categorised the efficacy for four interventions, based on information relating to the effectiveness and safety of: flexible ureteroscopy (combined with snare or basket or laser lithotripsy) versus expectant management, flexible ureteroscopy (combined with snare or basket or laser lithotripsy) versus extracorporeal shockwave lithotripsy, flexible ureteroscopy (combined with snare or basket or laser lithotripsy) versus percutaneous nephrolithotomy.

QUESTIONS

What are the effects of flexible ureteroscopy for the removal of renal stones? 4

INTERVENTIONS

FLEXIBLE URETEROSCOPY FOR RENAL STONES

Unknown effectiveness

Flexible ureteroscopy versus expectant management New 4

Flexible ureteroscopy versus extracorporeal shockwave lithotripsy (both may be effective at removing stones; however, insufficient evidence from RCTs as to which is most effective and in what circumstances). New . . 4

Flexible ureteroscopy versus percutaneous nephrolithotomy (both may be effective at removing stones; however, insufficient evidence from RCTs as to which is most effective and in what circumstances) New 8

Key points

- Kidney stones develop when crystals separate from the urine and aggregate within the kidney papillae, renal pelvis, or ureter.

  The age of peak incidence for stone disease is 20 to 40 years, although stones are seen in all age groups. There is a male to female ratio of 3:2.
- For kidney stones, percutaneous nephrolithotomy (PCNL), ureteroscopy, and extracorporeal shockwave lithotripsy (ESWL) are all options for treatment.
- Miniaturisation and the development of flexible ureteroscopes have broadened the potential indications and success rates for ureteroscopy. We have attempted to examine in detail the best evidence regarding the efficacy of flexible ureteroscopy, as it compares to established treatment options such as PCNL and ESWL.
- We searched for RCTs comparing flexible ureteroscopy versus expectant management, PCNL, or ESWL in people with kidney stones.
- We found four small RCTs of sufficient quality. The overall quality of evidence was weak.

  The populations included in the trials differed (in terms of stone size, location, and age of participant), as did the exact operative techniques employed.

  Three of the four studies were undertaken at a single centre, which may limit the generalisability of results.

  We only included trials with a minimum of 3 months' follow-up. However, we found no longer term results.

  It was, therefore, difficult to draw robust conclusions.
- There is a lack of large high-quality trials in this field to inform clinical practice. However, the difficulties of undertaking trials in this area should not be underestimated.

Clinical context

GENERAL BACKGROUND

Kidney stones develop when crystals precipitate out from the urine and aggregate within the kidney papillae, renal pelvis, or ureter. The most common type of stones are calcium-containing stones, which are usually formed of calcium oxalate and, less commonly, of calcium phosphate. Other metabolic stones include uric acid, cystine, and xanthine

stones.This overview assesses the effects of treatments for the removal of asymptomatic or symptomatic renal stones.

FOCUS OF THE REVIEW

The technologies for the treatment of kidney stones have evolved such that minimally invasive techniques are the norm. Evidence regarding the efficacy of modern and now widely available techniques such as flexible ureteroscopy has been lacking. We have attempted to examine in detail the best evidence regarding the efficacy of flexible ureteroscopy as it compares with more established treatment options such as percutaneous nephrolithotomy (PCNL) and extracorporeal shockwave lithotripsy (ESWL).

COMMENTS ON EVIDENCE

There remains a paucity of high-quality evidence regarding flexible ureteroscopy. The evidence that exists is also somewhat imperfect in its comparison techniques and should be judged accordingly. Nevertheless, the identified RCTs represent the best evidence available.

SEARCH AND APPRAISAL SUMMARY

The update literature search for this overview was carried out from the date of the last search, June 2011, to May 2014. For more information on the electronic databases searched and criteria applied during assessment of studies for potential relevance to the overview, please see the Methods section. After deduplication and removal of conference abstracts, 118 records were screened for inclusion in the overview. Appraisal of titles and abstracts led to the exclusion of 99 studies and the further review of 18 full publications. Of the 18 full articles evaluated, one systematic review and four RCTs were added at this update.

DEFINITION

Nephrolithiasis is the presence of stones within the kidney; **urolithiasis** is a more general term for stones anywhere within the urinary tract. Urolithiasis is usually categorised according to the anatomical location of the stones (i.e., renal calyces, renal pelvis, ureteric, bladder, and urethra). **Diagnosis** Diagnosis is usually based on clinical history, supported by investigations with diagnostic imaging. Kidney stones that remain in the kidney are frequently asymptomatic. However, they can become clinically evident due to obstruction, pain (often severe in nature), renal angle tenderness, haematuria, or digestive symptoms (e.g., nausea, vomiting, or diarrhoea). [1] The cause and chemical composition of a stone may have some bearing on its diagnosis, management, and, particularly, on prevention of recurrence. Although the choices for surgical management in general remain the same for all types of stone disease, the recognition of a specific cause, such as recurrent infection with a urease-producing organism for struvite stones or cystinuria for cystine stones, will inform further management. **Differential diagnosis** Bleeding within the urinary tract may present with identical symptoms to kidney stones, particularly if there are blood clots present within the renal pelvis or ureter. Other differential diagnoses include urinary tract infection (which may be concurrent), ureteropelvic junction obstruction, and urothelial carcinoma. Patients with papillary cell necrosis (which may occur in diabetes or sickle cell disease) may also present with renal colic. **Included studies** This overview assesses the effects of treatments only for the removal of asymptomatic or symptomatic renal stones. It excludes pregnant women, in whom some diagnostic procedures and treatments for stone removal may be contraindicated, and people with significant comorbidities (including severe cardiovascular and respiratory conditions) who may be at increased risk when having general anaesthesia. We have included studies examining the effects of flexible ureteroscopy alone (that could be combined with stone removal via snare or basket) or that also used laser lithotripsy. We have excluded studies undertaken in people with ureteric stones.

INCIDENCE/ PREVALENCE

The age of peak incidence for stone disease is 20 to 40 years, although stones are seen in all age groups. [2] The male predominance of stone disease may be decreasing, with recent reports of male to female ratio being approximately 3:2. [3] In North America, calcium oxalate stones (the most common variety) have a recurrence rate of 10% at 1 year and 35% at 5 years after the first episode of kidney stone disease. [2]

AETIOLOGY/ RISK FACTORS

Kidney stones develop when crystals precipitate out from the urine and aggregate within the kidney papillae, renal pelvis, or ureter. The most common type of stones are calcium-containing stones, which are usually formed of calcium oxalate, and less commonly of calcium phosphate. Other metabolic stones include uric acid, cystine, and xanthine stones. There are also infection stones, or 'struvite' stones, which contain a mixture of magnesium, ammonium, and phosphate, and are associated with urease-forming organisms such as *Klebsiella* or *Proteus* species. Predisposing factors for stone formation include dehydration, lifestyle, geographical location (dry arid climate), and certain specific risk factors. These factors may include anatomical/structural abnormalities (e.g., ureteropelvic junction obstruction, urinary diversion surgery, horseshoe kidney, calyceal di-

verticulum), and underlying metabolic conditions (e.g., cystinuria, oxaluria, gout), certain drugs, and urease-producing infective organisms.

PROGNOSIS

Most kidney stones that pass into the ureter pass within a few days to several weeks with expectant treatment (including adequate fluid intake and analgesia). Some kidney stones are asymptomatic and remain in the kidney, but may continue to grow in size. Expectant (conservative) management is considered on an individual basis in people with stones that are asymptomatic, mildly symptomatic, small, or in people with significant comorbidities, for whom the risks of treatment may outweigh the benefits. A stone causing chronic obstruction in the kidney may lead to hydronephrosis, renal atrophy, urinary infection, perinephric abscess, or urosepsis. Drainage of an infected obstructed kidney is a medical emergency. Infection may also occur after invasive procedures for stone removal. Some of these complications may cause kidney damage and compromised renal function. [4]

AIMS OF INTERVENTION

To render people free of stones; and to prevent the development of the complications of stone disease, with minimal adverse effects.

OUTCOMES

Removal of stones stone-free rate (proportion of people becoming stone free, assessed radiologically), including time to becoming stone free (duration of passing stone fragments); **treatment failure** (defined as no change in the stone, or the presence of large stone fragments, even if asymptomatic); **need for additional invasive procedures**; **recovery time after surgery**, including duration of hospital stay and time to return to normal activities or return to work; **recovery time** (for non-surgical interventions); **pain** (need for additional analgesia and re-admission to hospital); **adverse effects**.

METHODS

Search strategy *BMJ Clinical Evidence* search and appraisal May 2014. Databases used to identify studies for this systematic overview include: Medline 1966 to May 2014, Embase 1980 to May 2014, The Cochrane Database of Systematic Reviews, 2014, issue 5 (1966 to date of issue), the Database of Abstracts of Reviews of Effects (DARE), and Health Technology Assessment (HTA). **Inclusion criteria** Study design criteria for inclusion in this overview were systematic reviews and RCTs published in English and containing 50 or more individuals, of whom more than 80% were followed up. There was a minimum length of 3 months' follow-up required. We included all studies described as 'open', 'open label', or not blinded. *BMJ Clinical Evidence* does not necessarily report every study found (e.g., every systematic review). Rather, we report the most recent, relevant, and comprehensive studies identified through an agreed process involving our evidence team, editorial team, and expert contributors. **Evidence evaluation** A systematic literature search was conducted by our evidence team, who then assessed titles and abstracts, and finally selected articles for full text appraisal against inclusion and exclusion criteria agreed a priori with our expert contributors. In consultation with the expert contributors, studies were selected for inclusion and all data relevant to this overview extracted into the benefits and harms section of the overview. In addition, information that did not meet our predefined criteria for inclusion in the benefits and harms section, may have been reported in the 'Further information on studies' or 'Comment' section. **Adverse effects** All serious adverse effects, or those adverse effects reported as statistically significant, were included in the harms section of the overview. Pre-specified adverse effects identified as being clinically important were also reported, even if the results were not statistically significant. Although *BMJ Clinical Evidence* presents data on selected adverse effects reported in included studies, it is not meant to be, and cannot be, a comprehensive list of all adverse effects, contraindications, or interactions of included drugs or interventions. A reliable national or local drug database must be consulted for this information. **Comment and Clinical guide sections** In the Comment section of each intervention, our expert contributors may have provided additional comment and analysis of the evidence, which may include additional studies (over and above those identified via our systematic search) by way of background data or supporting information. As *BMJ Clinical Evidence* does not systematically search for studies reported in the Comment section, we cannot guarantee the completeness of the studies listed there or the robustness of methods. Our expert contributors add clinical context and interpretation to the Clinical guide sections where appropriate. **Structural changes this update** At this update, we have removed the following previously reported questions: What are the effects of interventions for stone removal in people with asymptomatic kidney stones? What are the effects of interventions to remove symptomatic ureteric stones? What are the effects of interventions for the management of acute renal colic? **Data and quality** To aid readability of the numerical data in our overviews, we round many percentages to the nearest whole number. Readers should be aware of this when relating percentages to summary statistics such as relative risks (RRs) and odds ratios (ORs). *BMJ Clinical Evidence* does not report all methodological details of included studies. Rather, it reports by exception any methodological issue or more general issue which may affect the weight a reader may put on an individual study, or the generalisability of the result. These issues may be reflected in the overall GRADE analysis. We have performed a GRADE evaluation of the quality of evidence for interventions included in this

review (see table, p 13). The categorisation of the quality of the evidence (high, moderate, low, or very low) reflects the quality of evidence available for our chosen outcomes in our defined populations of interest. These categorisations are not necessarily a reflection of the overall methodological quality of any individual study, because the Clinical Evidence population and outcome of choice may represent only a small subset of the total outcomes reported, and population included, in any individual trial. For further details of how we perform the GRADE evaluation and the scoring system we use, please see our website (www.clinicalevidence.com).

QUESTION **What are the effects of flexible ureteroscopy for the removal of renal stones?**

OPTION **FLEXIBLE URETEROSCOPY WITH OR WITHOUT LASER LITHOTRIPSY VERSUS EXPECTANT MANAGEMENT** New

- For GRADE evaluation of interventions for Kidney stones: flexible ureteroscopy, see table, p 13 .
- We found no direct evidence from RCTs on the effects of flexible ureteroscopy with or without laser lithotripsy versus expectant management.

Benefits and harms

Flexible ureteroscopy versus expectant management:

We found no systematic review or RCTs.

Comment: Although, intuitively, ureteroscopy may be of benefit in selected people with renal calculi, there are no studies available to support this over expectant management.

Clinical guide

There are no studies to support flexible ureteroscopy over expectant management. However, non-RCT data suggest that ureteroscopy is feasible in people with renal stones up to 2 cm in length. [5]

OPTION **FLEXIBLE URETEROSCOPY WITH OR WITHOUT LASER LITHOTRIPSY VERSUS EXTRACORPOREAL SHOCKWAVE LITHOTRIPSY** New

- For GRADE evaluation of interventions for Kidney stones: flexible ureteroscopy, see table, p 13 .
- We found two small RCTs, one of which was terminated early. One RCT was a multicentre study, the other was undertaken at a single site.
- Ureteroscopy and extracorporeal shockwave lithotripsy (ESWL) may be comparably effective in treating renal stones. Ureteroscopy may be associated with fewer procedures and more complications than ESWL.

Benefits and harms

Flexible ureteroscopy versus ESWL:

We found one systematic review (search date 2009). [6] The review included one small multi-centre RCT undertaken in 19 participating centres in the US (see Further information on studies). [7] The RCT included adults with isolated lower pole kidney stones in whom treatment was indicated (pain, infection, haematuria, local obstruction, and stone growth). We have reported the results directly from the original RCT. [7] We found one subsequent RCT, which included preschool children, none of whom had previous kidney stone treatment. [8] The RCT reported that all participants "presented with an initial stone episode", but did not further report on pre-operative symptoms. The RCT was undertaken in a single institution in Egypt (see Further information on studies). [8]

Removal of stones

Flexible ureteroscopy compared with ESWL We don't know whether flexible ureteroscopy (alone or with semi-rigid ureteroscopy) and ESWL differ in effectiveness at increasing the proportion of participants who are stone free at 3 months in adults with isolated symptomatic lower pole calculi less than 10 mm in size or in children with renal stones 10–12 mm in size (very low-quality evidence).

Ref (type)	Population	Outcome, Interventions	Results and statistical analysis	Effect size	Favours
Removal of stones					
[7] RCT	78 adults, mean age about 50 years, with isolated symptomatic lower pole calculi <10 mm in size In review [6]	**Proportion of people stone free , 3 months** 9/26 (35%) with ESWL 16/32 (50%) with flexible ureteroscopy	P= 0.92	⟷	Not significant
[8] RCT	60 children, mean age 2.4 years, range 1–6 years, renal stones 10–20 mm maximum dimension	**Proportion of participants stone-free , 3 months** 28/30 (93%) with ESWL 29/30 (97%) with ureteroscopy Reported results are after a mean of 1.4 procedures/participant for ESWL and 1 procedure/patient for ureteroscopy	P = 0.999 Intervention used semi-rigid and flexible ureteroscope (see Further information on studies)	⟷	Not significant

Treatment failure

No data from the following reference on this outcome. [7] [8]

Need for additional invasive procedures

Flexible ureteroscopy compared with ESWL We don't know whether flexible ureteroscopy (alone with with semi-rigid ureteroscopy) and ESWL differ in effectiveness at decreasing the need for additional treatments in adults with isolated symptomatic lower pole calculi less than 10 mm in size or in children with renal stones 10–20 mm in size (very low-quality evidence).

Ref (type)	Population	Outcome, Interventions	Results and statistical analysis	Effect size	Favours
Need for invasive procedures					
[7] RCT	78 adults, mean age about 50 years, with isolated symptomatic lower pole calculi <10 mm in size In review [6]	**Secondary treatments** 5 cases with ESWL 2 cases with flexible ureteroscopy Absolute numbers not reported Re-treatments (ESWL or ureteroscopy) were for target stone re-treatment and for obstructing ureteral fragments	Reported as not significant P value not reported	⟷	Not significant
[8] RCT	60 children, mean age 2.4 years, range 1–6 years, renal stones 10–20 mm maximum dimension	**Proportion of participants requiring re-treatment** 9 participants with ESWL 0 participants with ureteroscopy 2 participants with ESWL required a third procedure; 1 patient required pre-ureteroscopy stent placement, but did not then need a second procedure	Significance not reported Intervention used semi-rigid and flexible ureteroscope (see Further information on studies)		

Recovery time after surgery

Flexible ureteroscopy compared with ESWL ESWL may be more effective than flexible ureteroscopy at reducing the time taken to return to non-strenuous activity and work, in adults with isolated symptomatic lower pole calculi less than 10 mm in size, and it may also be more effective than ureteroscopy (using semi-rigid and flexible ureteroscopy) at reducing hospital stay in children with renal stones 10–20 mm in size (very low-quality evidence).

Ref (type)	Population	Outcome, Interventions	Results and statistical analysis	Effect size	Favours
Duration of hospital stay					
[7] RCT	78 adults, mean age about 50 years, with isolated symptomatic lower pole calculi <10 mm in size In review [6]	**Mean hospital stay** 0 days with ESWL 0.06 days with flexible ureteroscopy Absolute numbers not reported	P = 0.68	⟷	Not significant
[8] RCT	60 children, mean age 2.4 years, range 1–6 years, renal stones 10–20 mm maximum dimension	**Hospital stay** 6 hours with ESWL 12 hours with ureteroscopy	P <0.0001 Intervention used semi-rigid and flexible ureteroscope (see Further information on studies)	○○○	ESWL
Time to return to normal activities					
[7] RCT	78 adults, mean age about 50 years, with isolated symptomatic lower pole calculi <10 mm in size In review [6]	**Mean days to return to non-strenuous activity** 3.2 with ESWL 7.9 with flexible ureteroscopy Absolute numbers not reported	P = 0.021	○○○	ESWL
[7] RCT	78 adults, mean age about 50 years, with isolated symptomatic lower pole calculi <10 mm in size In review [6]	**Mean days to return to work** 3.3 with ESWL 8.5 with flexible ureteroscopy	P = 0.003	○○○	ESWL

Pain

Flexible ureteroscopy compared with ESWL ESWL may be more effective than flexible ureteroscopy at reducing the number of postoperative pills taken (outcome not further defined) in adults with isolated symptomatic lower pole calculi less than 10 mm in size, but the evidence was very weak (very low-quality evidence).

Ref (type)	Population	Outcome, Interventions	Results and statistical analysis	Effect size	Favours
Pain					
[7] RCT	78 adults, mean age about 50 years, with isolated symptomatic lower pole calculi <10 mm in size In review [6]	**Postoperative pain pills taken (not further defined)** 5.6 with ESWL 14.7 with flexible ureteroscopy Absolute numbers not reported	P = 0.015 Further details of measure (including timescale) not reported	○○○	ESWL

No data from the following reference on this outcome. [8]

Adverse effects

Ref (type)	Population	Outcome, Interventions	Results and statistical analysis	Effect size	Favours
Adverse effects					
[7]	78 adults, mean age about 50	**Adverse effects**			

Ref (type)	Population	Outcome, Interventions	Results and statistical analysis	Effect size	Favours
RCT	years, with isolated symptomatic lower pole calculi <10 mm in size In review [6]	with ESWL with ureteroscopy There was 1 intra-operative complication with ESWL (inability to target the stone) and 7 intra-operative complications with ureteroscopy (failed access in 5 people and ureteric perforation in 2 people); there were 7 postoperative complications in each group (further details not reported)			
[8] RCT	60 children, mean age 2.4 years, range 1–6 years, renal stones 10–20 mm maximum dimension	**Proportion of people with complications , 3 months** with ESWL with ureteroscopy Absolute results not reported The RCT reported that no major complications were noted in either group and no child received blood transfusion	Intervention used semi-rigid and flexible ureteroscope (see Further information on studies)		

Further information on studies

[6] *Methods* The review reported that, in the included RCT, 78 people were initially randomised, but 11 people dropped out of the study before treatment, and 67 people were treated on protocol. Of the people treated on protocol, 58/67 (87%) were analysed for stone removal after 3 months. Reasons for the 11 dropouts included stone movement out of the lower pole, procedure refused, insurance issues, medical reasons, and identification of a renal mass (further numerical details not reported). Allocation concealment was not stated, and the level of blinding of outcome and data assessors was not stated. The RCT was funded by a medical device company. *Population included* The RCT included adults with symptomatic isolated 1 cm or less lower pole stones. *Techniques used* The review reported that nine different lithotripters were used, the two most common being Doli-S (9 people treated) and HM3 (4 people treated). The ureteroscopes used included 7.5 Fr and Flex-X, ACMI Dur 8 and Dur 8-Elite, and URF-P3. It reported that dilatation of the intramural ureter was performed as needed, and the use of a ureteral access sheath, intact stone retrieval versus intracorporeal lithotripsy, and stent placement were left to investigator discretion. In the ureteroscopy arm, 17% of people had balloon dilation of the intramural ureter and in 69% a ureteral access sheath was used (absolute numbers not reported). The RCT reported that in the ureteroscopy arm, that 7/35 (20%) stones were removed intact, while in 23/35 (66%) the stone was fragmented using a holmium:YAG laser. [7] *Further comment on robustness of evidence* The RCT noted that it may have been underpowered to demonstrate a clinically important difference between groups. It reported that initial power calculations suggested that 50 people were needed per treatment arm. However, interim results after about 35 completed people per group revealed no significant difference in stone-free rate, and the study was terminated.

[8] *Methods* The analysis included all randomised participants. The method of randomisation was described, allocation was done by concealment rather than blinding, and it was unclear whether outcome assessment was blinded. Population included: during preoperative assessment, 14 participants had a urinary tract infection treated with antibiotics, 35 participants (58%) had a metabolic disorder that included hypercalciuria (18 participants), hyperuricaemia (11 participants), and hyperoxaluria (6 participants). The stone sites included pelvis (32 participants), pelvis and calyx (16 participants), and calyx (12 participants). *Techniques used* The same lithotripter was used (Modularis Variostar Lithotripter) under general anaesthesia and all procedures were undertaken by a single urologist. In the second group, access was achieved through hydrodilatation assisted by a hand irrigation pump (balloon dilation or ureteral access sheath not used). Fragmentation was performed using a holmium:YAG laser. When fragmentation was complete or a stone no longer accessible by the semi-rigid scope, the flexible Flex-X2 ureteroscope was introduced. The RCT reported that the surgical team was experienced with this technique in adults. *Further comment on robustness of evidence* The RCT noted that the main limitation of the study was the small number of participants, possibly because it was a single-site study; another limitation was the short follow-up.

Comment: Ureteroscopy may be as effective as ESWL at treating symptomatic renal stones, although the RCTs assessing this were probably underpowered to show a statistically significant difference. Ureteroscopy is associated with fewer procedures, but may have a higher complication rate than ESWL. The superiority of one technique over the other is unclear. [7]

Clinical guide
Both ureteroscopy and ESWL are feasible options for treating renal stones.

OPTION FLEXIBLE URETEROSCOPY WITH OR WITHOUT LASER LITHOTRIPSY VERSUS PERCUTANEOUS NEPHROLITHOTOMY New

- For GRADE evaluation of interventions for Kidney stones: flexible ureteroscopy, see table, p 13 .
- We found two small RCTs comparing flexible ureteroscopy with percutaneous nephrolithotomy (PCNL).
- Both studies were conducted in single tertiary care centres.
- Both flexible ureteroscopy and PCNL may be effective at removing kidney stones; however, we found insufficient evidence from RCTs as to which is most effective and in what circumstances.

Benefits and harms

Flexible ureteroscopy versus PCNL:

We found two RCTs. [9] [10] One RCT compared flexible ureteroscopy with micro-PCNL in a single tertiary care urological hospital in Western India (see Further information on studies). [9] The other RCT compared PCNL with semi-rigid and flexible ureteroscopy in a single tertiary care centre in Poland (see Further information on studies). [10] Neither RCT reported on pre-operative symptoms.

Removal of stones

Flexible ureteroscopy compared with PCNL PCNL may be more effective than ureteroscopy (including semi-rigid and flexible procedure) at reducing the presence of stones and stone debris at three weeks following discharge in adults with a single stone in renal pelvis over 2 cm, but we don't know about longer term results. Flexible ureteroscopy and PCNL may be equally effective at increasing complete stone clearance at 3 months in adults presenting with renal calculi less than 1.5 cm in size; however, evidence was limited (very low-quality evidence).

Ref (type)	Population	Outcome, Interventions	Results and statistical analysis	Effect size	Favours
Removal of stones					
[9] RCT	70 adults, mean age 39–44 years, presenting with renal calculi <1.5 cm	**Proportion of people with complete stone clearance , 3 months** 34/35 (98%) with micro-PCNL 33/35 (94%) with flexible ureteroscopy	P = 1.0	⟷	Not significant
[10] RCT	66 adults, mean age 52–53 years, single stone in renal pelvis, >2 cm	**Presence of stone at radiography (stone debris also included), 3 weeks after discharge** 2/32 (6%) with PCNL 8/32 (25%) with ureteroscopy	P = 0.03 Intervention used semi-rigid and flexible ureteroscope (see Further information on studies) The RCT reported that people were followed up and had an IVU at 3 months, but did not report on stone clearance beyond 3 weeks after discharge	○○○	PCNL

Treatment failure

No data from the following reference on this outcome. [9] [10]

Need for additional invasive procedures

Flexible ureteroscopy compared with PCNL Flexible ureteroscopy (including semi-rigid and flexible procedure) and PCNL may be equally effective at reducing the need for re-treatment; however, evidence was limited (very low-quality evidence).

Ref (type)	Population	Outcome, Interventions	Results and statistical analysis	Effect size	Favours
Need for further procedure					
[9] RCT	70 adults, mean age 39–44 years, presenting with renal calculi <1.5 cm	**Auxiliary procedures** 2 people with micro-PCNL 0 people with flexible ureteroscopy	P = 0.151	⟷	Not significant
[10] RCT	66 adults, mean age 52–53 years, single stone in renal pelvis, >2 cm	**People needing re-treatment** 2/32 (6%) with PCNL 4/32 (13%) with ureteroscopy In the PCNL group, 2 people had residual stones (6 mm and 8 mm) in the middle calyx; in the ureteroscopy group, 4 people had residual stones (4–5 mm) in the lower calyx	P value not reported Intervention used semi-rigid and flexible ureteroscope (see Further information on studies)		

Recovery after surgery

Flexible ureteroscopy compared with PCNL Flexible ureteroscopy (including semi-rigid and flexible procedures) may be more effective than PCNL at reducing mean hospital stay in adults with a single stone in renal pelvis over 2 cm. Flexible ureteroscopy and PCNL may be equally effective at decreasing hospital stay in adults presenting with renal calculi less than 1.5 cm in size; however, evidence was limited (very low-quality evidence).

Ref (type)	Population	Outcome, Interventions	Results and statistical analysis	Effect size	Favours
Duration of hospital stay					
[9] RCT	70 adults, mean age 39–44 years, presenting with renal calculi <1.5 cm	**Mean hospital stay** 57 hours with micro-PCNL 49 hours with flexible ureteroscopy	P = 0.08	⟷	Not significant
[10] RCT	66 adults, mean age 52–53 years, single stone in renal pelvis, >2 cm	**Mean hospital stay** 11.3 days with PCNL 6.8 days with ureteroscopy	P < 0.001 Intervention used semi-rigid and flexible ureteroscope (see Further information on studies)	○○○	ureteroscopy

Pain

Flexible ureteroscopy compared with PCNL Flexible ureteroscopy or ureteroscopy, including a semi-rigid and a flexible procedure, may be more effective than PCNL or micro-PCNL at reducing pain scores at up to 24 hours after the procedure, but we don't know about pain scores through the duration of the immediate postoperative period (very low-quality evidence).

Ref (type)	Population	Outcome, Interventions	Results and statistical analysis	Effect size	Favours
Pain					
[9] RCT	70 adults, mean age 39–44 years, presenting with renal calculi <1.5 cm	**Mean pain visual analogue score (scale 1–10) , at 6 hours** 4.8 with micro-PCNL 3.8 with flexible ureteroscopy	P = 0.003	○○○	flexible ureteroscopy

Ref (type)	Population	Outcome, Interventions	Results and statistical analysis	Effect size	Favours
[9] RCT	70 adults, mean age 39–44 years, presenting with renal calculi <1.5 cm	**Mean pain visual analogue score (scale 1–10) , at 12 hours** 3.4 with micro-PCNL 2.4 with flexible ureteroscopy	P = 0.009	○○○	flexible ureteroscopy
[9] RCT	70 adults, mean age 39–44 years, presenting with renal calculi <1.5 cm	**Mean pain visual analogue score (scale 1–10) , at 24 hours** 1.9 with micro-PCNL 1.6 with flexible ureteroscopy	P = 0.045	○○○	flexible ureteroscopy
[10] RCT	66 adults, mean age 52–53 years, single stone in renal pelvis, >2 cm	**Mean pain (measured by VAS – scale not further defined) , day after the procedure (further details not reported)** 2.65 with PCNL 1.10 with ureteroscopy	P <0.001 Intervention used semi-rigid and flexible ureteroscope (see Further information on studies) The RCT also reported that the mean amount of pethidine administered was significantly lower in the ureteroscopy group	○○○	ureteroscopy

Adverse effects

Ref (type)	Population	Outcome, Interventions	Results and statistical analysis	Effect size	Favours
Adverse effects					
[9] RCT	70 adults, mean age 39–44 years, presenting with renal calculi <1.5 cm	**Postoperative fever** 3 people with micro-PCNL 4 people with flexible ureteroscopy	P = 1.0 No person developed urosepsis	⟷	Not significant
[9] RCT	70 adults, mean age 39–44 years, presenting with renal calculi <1.5 cm	**Postoperative haemoglobin drop** 0.96 g/dL with micro-PCNL 0.56 g/dL with flexible ureteroscopy	P <0.001 No person required a blood transfusion	○○○	flexible ureteroscopy
[9] RCT	70 adults, mean age 39–44 years, presenting with renal calculi <1.5 cm	**Postoperative mild haematuria** 5 people with micro-PCNL 0 people with flexible ureteroscopy	P = 0.054 The RCT reported that haematuria last for 2 hours (3 people) and 8 hours (2 people) which subsided on its own	⟷	Not significant
[9] RCT	70 adults, mean age 39–44 years, presenting with renal calculi <1.5 cm	**Adverse effects** with micro-PCNL with flexible ureteroscopy Intra-operatively there was a minor pelvic perforation in 1 person with micro-PCNL that was managed by insertion of JJ stent; 1 person in each group required conversion to miniperc			
[10] RCT	66 adults, mean age 52–53 years, single stone in renal pelvis, >2 cm	**Mean % haemoglobin drop** 12% with PCNL 6% with ureteroscopy	P <0.001 Intervention used semi-rigid and flexible ureteroscope (see Further information on studies)	○○○	ureteroscopy

Ref (type)	Population	Outcome, Interventions	Results and statistical analysis	Effect size	Favours
[10] RCT	66 adults, mean age 52–53 years, single stone in renal pelvis, >2 cm	**Blood transfusion** 5/32 (16%) with PCNL 1/32 (3%) with ureteroscopy	The RCT reported that it adopted a 15% haematocrit drop as a single indication for blood transfusion; the normal transfusion rate for PCNL in the department, in general, was lower than this	⟷	Not significant
[10] RCT	66 adults, mean age 52–53 years, single stone in renal pelvis, >2 cm	**Fever (> 38°C)** 9/32 (28%) with PCNL 8/32 (25%) with ureteroscopy	P = 0.7 Intervention used semi-rigid and flexible ureteroscope (see Further information on studies)		

Further information on studies

[9] *Methods* The RCT reported that neither the participants nor investigators were blinded, and outcome assessment was not blinded. The analysis included all 70 people initially randomised. *Population included* The RCT included people aged 18 years or more with a single renal stone or multiple stones in the same line (which could be accessed in a single puncture), with the stone being less than 1.5 cm in size. The site of the stone was mainly in the pelvis (27 people) or lower calyx (32 people). *Techniques used* All procedures were performed under general anaesthesia. The RCT employed a Micro-PCNL procedure (microperc), which it reported was a recently described modified PCNL technique in which renal access and stone fragmentation are performed in a single step using a 4.85-F 'all seeing' needle. A 7-F ureteric catheter was used as part of the procedure, as was a 16-gauge three-part needle under ultrasonography and/or fluoroscopy guidance. The calculus was fragmented using a holmium:YAG laser. In the other group, the ureter was dilated with fascial dilators and a 12-F ureteric access sheath was placed. A 7.5-F Flex X2 flexible urteteroscope was used with a holmium laser with large fragments removed by a stone basket. Both procedures were performed by two senior surgeons.

[10] *Methods* Results were based on 64/66 (97%) people who were randomised. It reported participants were randomised "using the random number function", but did not report further details. The method of allocation concealment or level of blinding was not described. *Population included* The RCT reported that people received a diagnosis of renal pelvic stones in the outpatient clinic. It included people with a single stone located in the renal pelvis more than 2 cm in diameter. *Techniques used* The PCNL procedure involved a 5F ureteral catheter and a 30F Amplatz sheath with an ultrasonic lithotripter with continuous irrigation, with each procedure performed by the same surgeon. For ureteroscopy, the investigators used a semi-rigid ureteroscope 10/12F with a tapered tip. The ureteroscope was inserted within a 5F stent. Lithotripsy was accomplished using holmium laser with smaller stones evacuated with baskets or grabbers. If debris located in the middle or lower calyx was observed, the flexible ureteroscope was used for further lithotripsy. *Hospital stay* The RCT undertaken in Silesia noted that in most western countries, people may be discharged within 24 to 28 hours. However, the hospital stay was much longer in this trial. It reported that "our approach (from the procedural causes) is different, and therefore patients need a longer stay". It also reported another reason for longer stay may be the wide ureteroscope used. *Further comment on robustness of evidence* The RCT noted that limitations may include using a 15% haemocrit drop as a single indication for blood transfusion, the number of people in each arm was small, and it was a single-centre study.

Comment:

The Sabnis RCT [9] utilises microperc, which requires the use of laser and does not allow for suctioning of stone fragments. This technique also requires that the stones be in a single line or risk multiple punctures. The authors also limited their percutaneous procedures to stones smaller than 1.5 cm. The lack of obvious superiority in stone clearance with microperc for these stones less than 1.5 cm would suggest that ureteroscopy, where available, may be the more advantageous technique. Although, intuitively, PCNL would be more advantageous in patients with stones larger than 2 cm, this study does not address this.

The Bryniarski RCT [10] does address stones greater than 2 cm with a standard ultrasonic probe for PCNL. This study does demonstrate lower efficacy of stone clearance in these patients with ureteroscopy. Ureteroscopy was associated with a lower transfusion rate, hospital stay, and pain perception. The extremely long hospital stays for both arms may indicate differences in technique that may limit generalisability to western techniques.

GLOSSARY

Perinephric abscess Abscess lying within Gerota's fascia.

Hydronephrosis Dilatation of the renal pelvis and calyces, with or without dilatation of the ureter, which may result from an obstruction within the renal tract.

Very low-quality evidence Any estimate of effect is very uncertain.

SUBSTANTIVE CHANGES

Flexible ureteroscopy with or without laser lithotripsy versus expectant management New option. No evidence found. Categorised as 'unknown effectiveness'.

Flexible ureteroscopy with or without laser lithotripsy versus extracorporeal shockwave lithotripsy New option. One systematic review [6] and two RCTs added. [7] [8] Categorised as 'unknown effectiveness'.

Flexible ureteroscopy with or without laser lithotripsy versus percutaneous nephrolithotomy New option. Two RCTs added. [9] [10] Categorised as 'unknown effectiveness'.

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GRADE **Evaluation of interventions for Kidney stones: flexible ureteroscopy.**

Important outcomes	Need for additional invasive procedures, Pain, Recovery after surgery, Recovery time after surgery, Removal of stones, Treatment failure								
Studies (Participants)	Outcome	Comparison	Type of evidence	Quality	Consistency	Directness	Effect size	GRADE	Comment
What are the effects of flexible ureteroscopy for the removal of renal stones?									
2 (118) [7] [8]	Removal of stones	Flexible ureteroscopy versus ESWL	4	–3	0	–1	0	Very low	Quality points deducted for weak methods (allocation concealment, blinding), incomplete reporting of results, and sparse data; directness point deducted for unclear generalisability (single site 1 RCT; low follow-up 1 RCT; trial discontinued 1 RCT)
2 (118) [7] [8]	Need for additional invasive procedures	Flexible ureteroscopy versus ESWL	4	–3	0	–1	0	Very low	Quality points deducted for weak methods (allocation concealment, blinding), incomplete reporting of results, and sparse data; directness point deducted for unclear generalisability (single site 1 RCT; low follow-up 1 RCT; trial discontinued 1 RCT)
1 (unclear, no more than 118) [7] [8]	Recovery time after surgery	Flexible ureteroscopy versus ESWL	4	–3	0	–1	0	Very low	Quality points deducted for weak methods (allocation concealment, blinding), incomplete reporting of results, and sparse data; directness point deducted for unclear generalisability (single site 1 RCT; low follow-up 1 RCT; trial discontinued 1 RCT)
1 (unclear, no more than 78) [7]	Pain	Flexible ureteroscopy versus ESWL	4	–3	0	–2	0	Very low	Quality points deducted for weak methods (allocation concealment, blinding), incomplete reporting of results, and sparse data; directness points deducted for unclear generalisability (low follow-up and trial discontinued) and unclear outcome measurement
2 (134) [9] [10]	Removal of stones	Flexible ureteroscopy versus PCNL	4	–2	0	–2	0	Very low	Quality points deducted for weak methods (blinding, allocation concealment) and sparse data; directness points deducted for unclear generalisability (1 RCT different protocol [hospital stay] single-centre studies; 1 RCT used wide ureteroscope) and indirect comparisons
2 (134) [9] [10]	Need for additional invasive procedures	Flexible ureteroscopy versus PCNL	4	–2	0	–2	0	Very low	Quality points deducted for weak methods (blinding, allocation concealment) and sparse data; directness points deducted for unclear generalisability (1 RCT different protocol [hospital stay] single-centre studies; 1 RCT used wide ureteroscope) and no statistical analysis between groups
2 (134) [9] [10]	Recovery after surgery	Flexible ureteroscopy versus PCNL	4	–2	0	–1	0	Very low	Quality points deducted for weak methods (blinding, allocation concealment) and sparse data; directness point deducted for unclear generalisability (1 RCT different protocol [hospital stay] single-centre studies; 1 RCT used wide ureteroscope)

Important outcomes	Need for additional invasive procedures, Pain, Recovery after surgery, Recovery time after surgery, Removal of stones, Treatment failure								
Studies (Participants)	**Outcome**	**Comparison**	**Type of evidence**	**Quality**	**Consistency**	**Directness**	**Effect size**	**GRADE**	**Comment**
2 (134) [9] [10]	Pain	Flexible ureteroscopy versus PCNL	4	–2	0	–1	0	Very low	Quality points deducted for weak methods (blinding, allocation concealment) and sparse data; directness point deducted for unclear generalisability (1 RCT different protocol [hospital stay] single-centre studies; 1 RCT used wide ureteroscope)

We initially allocate 4 points to evidence from RCTs, and 2 points to evidence from observational studies. To attain the final GRADE score for a given comparison, points are deducted or added from this initial score based on preset criteria relating to the categories of quality, directness, consistency, and effect size. Quality: based on issues affecting methodological rigour (e.g., incomplete reporting of results, quasi-randomisation, sparse data [<200 people in the analysis]). Consistency: based on similarity of results across studies. Directness: based on generalisability of population or outcomes. Effect size: based on magnitude of effect as measured by statistics such as relative risk, odds ratio, or hazard ratio.